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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/719,410 | 12/12/2000 | Burkhard Goke | P03986US2 | 8826 |

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|---|---|
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| ART UNIT | PAPER NUMBER |
|---|---|
| 1653 | |

DATE MAILED: 10/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/719,410 | GOKE ET AL. | |
| | Examiner | Art Unit | |
| | Abdel A. Mohamed | 1653 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 July 2003* .

2a)☐ This action is **FINAL.** 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

## ACKNOWLEDGMENT OF PRIORITY, IDS, SEQUENCE LISTING, RESPONSE TO RESTRICTION REQUIREMENT, STATUS OF THE APPLICATIONAND CLAIMS

1. This application is filed under 35 U.S.C. 371 on 12/12/00 having a filing date of 5/7/99 of PCT/US99/10040. Acknowledgment is made of Applicant's claim for priority based on U.S. Provisional Application No. 60/089,044 having a filing date of 6/12/98. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119, which papers have been placed of record in the file. Also, the information disclosure statement (IDS) and Form PTO-1449 filed 3/12/01, the sequence listing filed 1/25/02 and the response to the restriction requirement filed 7/22/03 are acknowledged, entered and considered. Claims 1-40 are now pending in the application.

## ELECTION WITH TRAVERSE

2. Applicant's election with traverse of Group I (claims 10-38) in Paper No. 13 is acknowledged. The traversal is on the ground(s) that there is a close relationship between the subject matter of the Group I, II and III claims, there would be no serious burden on the Examiner to examine both sets of claims at this time. Claims 10-40 all relate to methods for treating various disorders using the same compound/composition. As such, there is a close relationship between the subject matter of these three sets of claims. It is believed that there would be no serious burden on the Examiner to examine all of claims 10-40 together at this time. The Examiner agrees Applicant's characterization with respect to Groups I-III that there is a close relationship between

the subject matter of these three sets of claims because they use the same compound/composition for treating the claimed disorders. Thus, the claims will be rejoined and examined together. Hence, the Office action is directed to the merits of claims 1-40.

## OBJECTIONS TO THE SPECIFICATION AND CLAIMS

3. The specification on pages 8 and 10 and claims 4-5, 13-14, and 27-28 are objected in the recitation "(SEQ. ID NO:1), (SEQ. ID NO:2), (SEQ. ID NO:3), (SEQ. ID NO:4), etc.". As required by 37 C.F.R. 1.821(c), each sequence set forth in the "Sequence Listing" shall be assigned a separate identifier written as SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, etc. Thus, appropriate correction is required.

## CLAIMS REJECTION-35 U.S.C. § 112$^{2nd}$ PARAGRAPH

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 17 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in the recitation the acronym "GLP-1". Use of full terminology at least in the first occurrence would obviate this rejection.

Claims 9, 17 and 31 are indefinite in the recitation "having a molecular weight of not greater than about 5000" because not greater than means ≤ 5000 "about" means can be > 5000, how much more than 5000 is about is unclear since the specification or the claim fails to provide guidance as to what measure to ascribe to the word "about". Further, the method used to determine the molecular weight was not identified since the molecular weight observed may vary slightly depending on the technique used in performing the analysis. Also, the molecular weight of "5000" should be identified whether it is in Dalton or Kilo Dalton. Appropriate correction is required.

**CLAIM REJECTION-35 U.S.C. § 102(b)**

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 and 39-40 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/08531.

WO 98/08531 discloses a composition comprising a compound from the group consisting of GLP-1, GLP-1 analogs, GLP-1 derivatives, and pharmaceutically acceptable salts thereof, at a dose effective to normalize blood glucose by increasing the glucose level in a patient with impaired glucose tolerance (IGT), wherein the GLP-1 is substituted and differs by one or more substitutions, and the amino acid sequences

does not differ by more than ten amino acids from the amino acid sequences of GLP-1 and wherein the receptor binding compound is GLP-1 (See e.g., pages 4 and 7 to 8) as directed to claims 1-3 and 6. Further, on pages 5, 6 and 10, the reference discloses SEQ ID NOS:3 and 4 (i.e., GLP-1 (1-37) and (7-36) amides) which are identical with SEQ ID NOS:1 and 2 of the reference, and as such meets the limitations of claims 4 and 5.

With respect to the limitations of claims 7 and 8, wherein the composition further comprises an agent which enhances the half-life *in vivo* of the compound and wherein the receptor binding compound is expressed by a polynucleotide. The reference clearly shows the preparation of pharmaceutical formulation comprising agents which enhance the half-life *in* vivo of the pharmaceutical formulation including the active agent GLP-1 (e.g., agents used to enhance half-life *in* vivo of the compound are disclosed on pages 16 and 17). The reference also shows the formulation of the amino acid portion of the active compound by methods known in the art, such as recombinant DNA technology, wherein the reference teaches the expression of the receptor binding compound by a polynucleotide (See e.g., pages 11-14 and 16-17) as directed to claims 7 and 8.

The cited reference above does not disclose the intended use of the composition for the treatment of IGT, although, the reference discloses the use of GLP-1 or analogs in treatment of myocardial infarction which meets the he limitations of claims 39 and 40; nevertheless, a statement of usefulness or contemplated use of a claimed compound or composition in a claim is usually given little weight in distinguishing over the prior art. *In re Maeder et al.* (CCPA 1964) 337 F2d 875, 143 USPQ 248; *In re Riden et al.* (CCPA 1963) 318 F2d 761, 138 USPQ 112; *In re Sinex* (CCPA 1962) 309 F2d 488, 135 USPQ 302. Further, it is well established that the intended use of a compound (e.g., a polypeptide or a protein or a glycoprotein) does not impart patentability to the

compound. *In re Spada,* 911 F.2d 705, 15 USPQ2d 1655 (Fed. Cir. 1990) (The discovery of a new property or use of a previously known composition, even when that property and use are unobvious from the prior art, can not impart patentability to claims to the known composition); *In re Pearson*, 494 F.2d 1399, 1403, 181 USPQ 641, 644 (CCPA 1974) (intended use of an old composition does not render composition claims patentable); *In re Zierden*, 411 F.2d 1325, 1328, 162 USPQ 102, 104 (CCPA 1969). Thus, in the absence of evidence to the contrary or specific structural limitations, the claimed composition/product disclosed including method of treating individual whose symptoms indicate increased risk of a cardiovascular event by administering the claimed composition thereof by the reference anticipates claims 1-8 and 39-40 as drafted.

**CLAIMS REJECTION-35 U.S.C. § 103(a)**

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/08531 taken with Rachman et al., (Diabetologia, Vol. 40, pp. 205-211, 1977).

The reference of WO 98/08531 as discussed above discloses a composition comprising a compound from the group consisting of GLP-1, GLP-1 analogs, GLP-1 derivatives, and pharmaceutically acceptable salts thereof, at a dose effective to normalize blood glucose by increasing the glucose level in a patient with impaired glucose tolerance (IGT), wherein the GLP-1 is substituted and differs by one or more substitutions, and the amino acid sequences does not differ by more than ten amino acids from the amino acid sequences of GLP-1 and wherein the receptor binding compound is GLP-1 (See e.g., pages 4 and 7 to 8) as directed to claims 1-3, 6, 11-12, 15, 25-26 and 29. Further, on pages 5, 6 and 10, the reference discloses SEQ ID NOS:3 and 4 (i.e., GLP-1 (1-37) and (7-36) amides) which are identical with SEQ ID NOS:1 and 2 of the reference, and as such meets the limitations of claims 4-5, 13-14 and 27-28.

With respect to the limitations of claims 7-8, 16, 19 and 30 wherein the composition further comprises an agent which enhances the half-life *in vivo* of the compound and wherein the receptor binding compound is expressed by a polynucleotide. The reference clearly shows the preparation of pharmaceutical formulation comprising agents which enhance the half-life *in* vivo of the pharmaceutical formulation including the active agent GLP-1 (e.g., agents used to enhance half-life *in* vivo of the compound are disclosed on pages 16 and 17). The reference also shows the formulation of the amino acid portion of the active compound by methods known in

the art, such as recombinant DNA technology, wherein the reference teaches the expression of the receptor binding compound by a polynucleotide (See e.g., pages 11-14 and 16-17) as directed to claims 7-8, 16, 19-20 and 30.

On page 18, the reference states that administration may be via any route known to be effective by the physician of ordinary skill and cites that parenteral administration is preferred. The reference continues to state that parenteral administration is commonly understood in the medical literature as the injection of a dosage form into the body by sterile syringe or some other mechanical device such as an infusion pump. Parenteral routes include intravenous, intramuscular, subcutaneous, intraperitoneal, etc., and as such meets the limitations of claims 18 and 32. Also, on page 20, the reference discloses the simultaneous administration of the effective amount of the composition in dosage ranges from 0.25 to 6 pmol/kg body weight/min, preferably from about 0.5 to about 1.2 pmol/kg/min, and as such meets the limitations of claims 22-23, and 33-34. The reference is mainly directed to a method of reducing mortality and morbidity after myocardial infraction by administering GLP-1 and a GLP-1 analog or derivative thereof at a dose effective to normalize blood glucose (See e.g. abstract, Examples 1and 2 and claims 1-13) as directed to claims 39 and 40.

The reference of WO 98/08531 differs from claims 1-40 in failing to teach a) wherein the receptor-binding compound is an organic molecule having a molecular weight of not greater than about 5000 (presumably Daltons); b) a biologically active analogue of GLP-1 in which combination of the substitutions, deletions and insertions in the amino acid sequence does not differ by more than ten or five amino acids from the amino acid sequence of GLP-1; and c) a method for treating an individual with IGT to control the development of non-insulin dependent diabetes mellitus (NIDDM) in a human by administering the composition claimed. Although, the prior art of WO

98/08531 clearly teaches the use of GLP-1 for the treatment of NIDDM, wherein the GLP-1 (7-36) amide or GLP-1 (7-37) exert a pronounced antidiabetogenic effect in insulin-dependent diabetics by stimulating insulin sensitivity and by enhancing glucose-induced insulin release at physiological concentrations thereby resulting in stimulation of insulin release, lowering glucose secretion, inhibiting gastric emptying and enhancing glucose utilization (See e.g., pages 3-4, 19 and Examples 1 and 2) as directed to claims 24 and 35-38. However, the reference of Rachman et al., study was performed in order to determine the feasibility and efficacy of continuous administration of GLP-1 in NIDDM. The study showed that continuous infusion of GLP-1 markedly improved both overnight and daytime glucose concentrations in subjects with NIDDM reduced plasma glucose concentrations and stimulated insulin secretion in IGT and NIDDM subjects, wherein GLP-1 restored the ability of β-cell to sense and respond to plasma glucose in all IGT subjects with a variable response who had already developed NIDDM. Also, the reference discloses the dosage of GLP-1 given was at a rate of 1.2 pmol/kg/min and the peptide comprises an amino acid sequence that differs from the sequence of GLP-1 peptide by one or more substitutions (See e.g., pages 205-206, Figures 1-4 and pages 209-210) as directed to claims 24-28 and 32-38. As to the limitations of a biologically active analogue of GLP-1 in which combination of the substitutions, deletions and insertions in the amino acid sequence does not differ by more than ten or five amino acids from the amino acid sequence of GLP-1; The primary reference of WO 98/08531 on pages 7 to 8 teaches the various substitutions of amino acids which differs by one or more substitutions, or the amino acid sequences does not differ by more than thirteen amino acids from the amino acid sequences of GLP-1 and wherein the receptor binding compound is GLP-1 (See e.g., pages 4 and 7 to 8) as directed to claims 2, 6, 11, 15, 25 and 29, in contrast, to the claimed invention which does not differ by more than five

amino acids or ten amino acids from the amino acid sequences of GLP-1. However, given the teachings of WO 98/08531, one of ordinary skill in the art would easily adjust or modify the number of amino acid in a given sequence according to the need because techniques for such replacement, insertion, or deletion are well know in the art to which this invention pertains. Further, in regard to the limitations wherein the receptor binding compound is an organic molecule having a molecular weight of not greater than about 5000, none of the prior art disclose the molecular weight of not greater than about 5000, however, both references disclose the same receptor binding compound, and as such, the molecular weight claimed is the expected property of the references receptor binding compound. Thus, the prior art meets the limitations of claims 9, 17 and 31.

With respect to the dosage ranges and mode of administrations, the ranges and mode of administrations disclosed in the prior art and claimed by Applicant overlap in scope as discussed above (See e.g., page 8 of the Office action), and as such, the selection of the appropriate dosages and route of administrations would have been *prima* facie obvious because where the general conditions of claims are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges or situations by routine experimentation.

Therefore, in view of the above and in view of the combined teachings of the prior art, one of ordinary skill in the art would have been motivated at he time the invention was made to employ a composition comprising a compound which binds to a receptor of GLP-1 and a pharmaceutical formulation thereof and to a method for treating an individual with IGT by administering effective amount of said composition thereof to reduce insulin resistance and its concomitant condition of cardiovascular disease. Thus, claims 1-40 are *prima facie* obvious over the combined teachings of the prior art, absence of sufficient objective factual evidence or unexpected results to the contrary.

## CITATION OF RELEVANT PRIOR ART

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Holst et al., (U.S. Patent No. 6,344,180) teach the use of GLP-1 for the detection of impaired β-cell function of individual as diagnostic indicator of IGT and a warning sign of diabetes.

## CONCLUSION AND FUTURE CORRESPONDENCE

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (703) 308-3966. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (703) 308-2923. The fax phone number for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Mohamed/AAM

October 17, 2003

Christopher S. F. Low

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